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Investigation of energy expenditure during walking in children with cerebral palsy and typically developing children using raw acceleration data

Master's thesis in Human Movement Science

Trondheim, June 2016

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ABSTRACT

Background: Children with cerebral palsy (CP) experience motor disabilities which can lead to difficulties when walking. This is apparent in lower walking speed and higher energy expenditure (EE) when walking compared to typically developing (TD) peers, in addition to more sedentary time and lower participation. EE estimations are often done in this group to investigate the effect of treatments. EE indicates the amount of energy used to perform a task and is commonly estimated from oxygen consumption (VO_2) measurements using indirect calorimetry. A less invasive method is desirable, and activity monitors are now being used for this purpose. They measure acceleration during movement and relate the output to EE.

Aim: To investigate if raw acceleration data can be used to estimate EE in children with CP and TD children during walking.

Methods: Fifteen typically developing (TD) children (mean age 10.0 yrs ± 1.7) and six children with CP (mean age 12.4 yrs ± 3.9, GMFCS level I-III) performed a five-minute walking test at preferred walking speed while wearing two Axivity AX3 activity monitors (lower back and mid-thigh) and portable indirect calorimetry equipment (Metamax II). Distance walked was recorded with a measuring wheel. EE and relative VO_2 was estimated from indirect spirometry and equations developed by Brandes et al. and Hildebrand et al, using vector magnitude (VM) from the acceleration signal as input.

Results: EE and relative EE values from indirect calorimetry and acceleration data were almost identical, overestimating with 0.1% and 4.5% for the TD children and 4.8 % and 2.3% for the children with CP. Both equations estimating relative VO_2 gave accurate estimations for the children with CP (1.2% and 3.4% overestimation), but a significant difference was seen between the relative VO_2 from acceleration data and the values obtained by indirect calorimetry for the TD children (12.9% and 14.1%). A large variation was found in the accuracy of the estimations for each participant, with wide limits of agreement in a Bland-Altman analysis. There was not found a statistical difference in VM for the groups. The VM showed little variation in the acceleration signal during the test period (mean range 0.06 g for the TD children and 0.082 g for the children with CP).

Conclusion: Accurate estimations of EE and relative VO_2 during walking can be made on group level for TD children and children with CP, using raw acceleration data, but not on individual level.

ABSTRAKT

Bakgrunn: Barn med cerebral parese (CP) opplever nevrologiske forstyrrelser, noe som ofte fører til problemer med gangfunksjonen. Dette er gjerne tydelig gjennom lavere hastighet og høyere energiforbruk under gange i forhold til funksjonsfriske jevnaldrende. I tillegg er barn med CP mer stillesittende i hverdagen enn de funksjonsfriske og deltar på færre fritidsaktiviteter. Estimering av energiforbruk brukes ofte for å undersøke effekten av behandling på denne gruppen. Energiforbruk indikerer mengden energi som brukes til å utføre en oppgave og estimeres vanligvis ut ifra målinger av oksygenopptak (VO_2) ved bruk av indirekte kalorimetri. Det er ønskelig å kunne bruke en mindre omfattende metode å estimere energiforbruk på og aktivitetsmonitorer brukes nå med dette formålet. De måler akselerasjonen under en bevegelse og relaterer signalet til energiforbruk.

Mål: Undersøke om råsignal fra akselerometer kan brukes til å estimere energiforbruk hos barn med CP og funksjonsfriske barn.

Metode: Femten funksjonsfriske barn (gjennomsnittsalder 10.0 år ± 1.7) og seks barn med CP (gjennomsnittsalder 12.4 ± 3.9 år, GMFCS nivå I-III) gjennomførte en fem minutter lang gangtest i normal, selvvalgt hastighet mens de hadde på seg to Axivty AX3 aktivitetsmonitorer (korsryggen og midt på lår) i tillegg til bærbart indirekte kalorimetriutstyr (Metamax II). Ganglengde ble målt med håndholdt målehjul. Energiforbruk og relativ VO_2 ble estimert ved bruk av indirekte kalorimetri og fra likninger utviklet av Brandes et al. og Hildebrand et al. med vektor magnitude (VM) som input fra akselerasjonssignalet.

Resultat: Energiforbruk og relativt energiforbruk fra indirekte kalorimetri og akselerasjonsdata var nærmest identiske og overestimerte kun med 0.1% og 4.5% for de funksjonsfriske og med 4.8% og 2.3% for barna med CP. Begge likningene som estimerte relativ VO_2 ga nøyaktige estimat for barna med CP (1.2% og 3.4% overestimering), men en signifikant forskjell ble funnet mellom relativ VO_2 estimert fra akselerasjonsdata og verdiene fra indirekte kalorimetri for de funksjonsfriske (12.9% og 14.1% overestimering). Store variasjoner fantes estimatene for hvor hver deltaker, med vide grenser for enighet (limits of agreement) i en Bland-Altman analyse. Det var ingen statistisk forskjell i VM mellom gruppene. VM viste til liten variasjon i akselerasjonssignalet under testperioden (gjennomsnittsrekkevidde 0.06 g for funksjonsfriske og 0.082 g for barna med CP).

Konklusjon: Nøyaktige estimeringer av energiforbruk og relativ VO_2 kan gjøres på et gruppenivå for funksjonsfriske og barn med CP, men å få nøyaktige estimeringen på individnivå er mer utfordrende.

ACKNOWLEDGEMENT

I would like to thank my supervisor professor Karin Roeleveld for her guidance and feedback, it has been of great help when writing this thesis. I also thank my co-supervisors post docs Siri Merete Brændvik and Ellen Marie Bardal for their advices and help with recruitment and data analysis.

A thank you is sent to Netherland and Maaike Eke for her help during the data collection and for making me better understand Matlab.

To my fellow students, Astrid Ustad and Ane Øvreness, I am very grateful for having you with me during long days at the lab and when writing. Thank you for making the days more fun and for sharing your thoughts and ideas, it is highly appreciated.

At last, a special thanks goes to all the children who participated in this study for their good efforts, and to their families for taking the time to come.

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ABBREVIATIONS

CI: Confidence interval

CP: Cerebral palsy

EC: Energy cost (J/kg/m)

EE: Energy expenditure (kJ/min or J/kg/min)

HR: Heart rate

O_2 cost: Oxygen cost (mL/kg/m)

SD: Standard deviation

TD: Typically developing

VM: Vector magnitude

VO_2: Oxygen consumption (L/min or mL/kg/min)

INTRODUCTION

Cerebral palsy (CP) is the most common cause of motor disabilities among children and is caused by a lesion in the brain before, during or shortly after birth.[1] It is described as a group of permanent disorders of the development of movement and posture causing activity limitations.[1] These motor problems can lead to difficulties when walking, which is apparent in lower walking speed and higher energy expenditure (EE) when walking compared to typically developing (TD) children.[2,3] The EE of a task indicates the amount of energy (in joule) used to perform the task.[4] Children with CP can expend up to three times the energy required for walking, and as a consequence of this, they tire easily and walk less.[4-6] This results in more sedentary time and lower participation in school and leisure activities compared to their TD peers.[7,8] The goal of many treatments for children with CP is on improving EE during walking and decrease the feeling of fatigue to increase their overall physical activity level.[6,9] To examine the effect of the treatments it is common to compare pre- and post-measurements of EE. The most common way to estimate EE is from oxygen consumption (VO_2) measurements using indirect calorimetry.[10] By combining it with information about distance walked, energy cost (EC) can be estimated.[11] EC is the amount of energy consumed per meter and is well accepted as an accurate indicator of walking efficiency.[11,12] Although widely used, VO_2 measurements have some challenges and limitations. One important note is that only during steady state and low to moderate intensities there is a direct and predictable relationship between VO_2 and energy expenditure.[13] For this reason, it is important that measurements take place after this state is reached. The duration of the test should therefore be longer than 2 minutes to ensure this.[14] The equipment used is expensive and time consuming to calibrate and prepare, in addition the measurements are limited to laboratory settings. More importantly, young children can experience fear or anxiety for wearing a mask, which can complicate or prevent correctly performed measures. For these reasons, a less extensive method to find EE is useful.

Accelerometers are monitors that measure the acceleration (in gravitational acceleration units *g*) they are exposed to and are thus mechanical measurements.[15] Because of this, they do not need to consider physiological factors such as reaching steady state during testing, which can reduce the test period. Depending on the type, accelerometers measure acceleration in one (vertical) to three orthogonal planes (vertical, mediolateral and anteroposterior).[16] When the

monitor is exposed to acceleration caused by a movement, it creates an electrical charge which generate a variable output voltage signal proportional to the applied acceleration.[15,16] Acceleration is defined as the change in velocity over time, and in this way quantifies the volume and intensity of movement.[17] Since the acceleration signal is related to the movement made, it also has a potential to be used to describe the amount of energy used to perform it. To do this, the relation between acceleration signal and EE must be determined. Previous studies have developed different estimation methods from the acceleration signal.[18] The majority of these focus on the use of activity counts. Activity counts are unit-less numerical values that are created by inbuilt software developed by the manufactores.[15,19] The software filters the acceleration signal and uses algorithms to sum up the output over a specified time period (normally ranging from 1 to 60 seconds).[15,19] Activity, age and gender specific cut-off values or thresholds are developed to relate the amount of activity counts to different intensities of physical activity and categories of energy expenditure.[16,19] The counts can also be used in regression models to estimate EE values.[20]

Previous validation studies have found a moderate to high correlation between EE estimated using activity counts and values measured by indirect calorimetry.[21-25] O'Neil et al. have studied the use of different types of accelerometers among children with CP, and have found a fair to good validity between activity counts and VO_2 measurements ($r = 0.67$, $p = <0.001$).[21] This finding was repeated in a later study where they also found that VO_2 and activity counts have a dose-response relationship.[22] The counts increased significantly as the intensity of the trials increased. Puyau et al. studied 32 children between 7-18 that performed a wide range of structured activities while wearing two types of activity monitors (Actiwatch and Actical).[25] They found that the activity counts accounted for the majority of the variability (about 80%) seen in physical activity specific EE. Although activity counts can be used to estimate EE, the method have clear weaknesses and limitations. Since the transformation of raw acceleration signal to activity counts is carried out in brand specific software, exactly how the signal is processed and analyzed to get the counts is unknown. In addition, many different cut-off values exist to classify intensity and EE. Overall, the use of activity counts in EE limits the utilization of the acceleration signal and reduces the comparability of studies on the field.

To avoid the mentioned disadvantages that follow from using activity counts, an approach is to base the analysis on raw acceleration data with clarification on how the signal is processed,

to enable reproduction of the method. This is also suggested by studies that investigate or review the use of accelerometers as focus areas for future research.[15,17,20] The procedure is currently little used. Reasons for this is that few of the accelerometers available give the user access to the raw, unfiltered, data. In addition, other methods to analyze the signal must be used, and less work exists on this area. As previously mentioned, some studies use regression models to estimate EE from activity counts. Similar methods can be used on raw acceleration data. One study that investigated this was Brandes et al.[26] They developed regression coefficients and prediction equations from acceleration data from 186 participants that wore a monitor (DynaPort) on their lower back while completing a physical activity course. This included walking at three different speeds (slow, normal and fast) for eight minutes each, in addition to stair walking and cycling. Hildebrand et al. also developed similar regression equations for relative VO_2 .[27] The equations were based on acceleration data from two monitors (ActiGraph and GENEActiv) placed on the hip. Thirty children were tested, performing eight structured activities, including walking at two different speeds and running. These equations look promising, but need to be evaluated to see if they manage to accurately estimate EE and relative VO_2 on others.

The aim of this study was to investigate if raw acceleration data from the Axivity AX3 activity monitors could be used to estimate EE in children with CP and TD children during walking. Existing equations from Brandes et al. and Hildebrand et al. are used for the estimations and the values compared against indirect calorimetry measurements to examine the accuracy and agreement between the methods.

METHODS

Participants

A total of 22 subjects were recruited to the study. Sixteen of these were TD children between 6 and 14 years, recruited trough the employees at St. Olavs University Hospital and the Norwegian University of Science and Technology in Trondheim, Norway. They were generally healthy with no contraindications or disorders that affect EE. Six children with CP between the age of 6 and 16 with Gross Motor Function Classification System (GMFSC)[28] levels I-III were also included. Five of these through the Children's Orthopedic at the Child and Youth Clinic at the hospital as they were sent to the gait laboratory for consultation, and one from an ongoing study on children with CP (The WE-study). They were all able to take

verbal instructions and to walk consistently for at least five minutes without assistant devices. A written consent was signed by both parents before the child was tested. They were informed that they at any time during the testing could withdraw from the study without giving a reason. The study was approved by the Regional Committee for Medical and Health Research Ethics.

Equipment

A stadiometer (Seca, Hamburg, Germany) was used to measure height and a digital scale (Seca, Hamburg, Germany) to measure weight. Distance walked during the test was measured using a standardized measuring wheel with 1.0 meter circumference (Blinken A/S, Gressvik, Norway). Heart rate was measured using Polar RS400 (Polar Electro Oy, Finland) and the associate chest strap with a heart rate monitor.

A portable indirect calorimeter, Metamax II (Cortex Biophysik GmbH, Leipzig, Germany) was used to measure VO_2 and calculate respiratory exchange ratio (RER). The Metamax measures the breathed volume through a flow turbine and contains oxygen (O_2) and carbon dioxide (CO_2) sensors that analyses the ventilated gas. Values are shown for every 10^{th} second. A calibration of the equipment was done according to the manufactures' instructions before each test. An ambulant air and a reference gas (15% O_2 and 5% CO_2) calibration was performed and the flow turbine was calibrated with a 3.00 liter syringe (Hans-Rudolph, Shawnee, KS).

Three Axivity AX3 (Axivity, Newcastle upon Thyne, UK) activity monitors were used. They are small (23 x 32.5 x 7.6 mm) and light (11 gram) and contain a MEMS triaxial accelerometer, NAND memory (512 MB), microprocessor and a temperature sensor.[29] Figure 1 show the orientation of the axis of the monitor. When attached, the x-axis is equaled to the vertical plane, the y-axis to the mediolateral plane and the z-axis to the anteroposterior plane. Before testing correct measuring time was set (day:hour:minute) in the software Omgui (version 1.0.0.28). A measuring range of ±8 g and sampling frequency of 200 Hz was used. Each monitor was put in a finger cot with a piece of double-sided tape closing it.

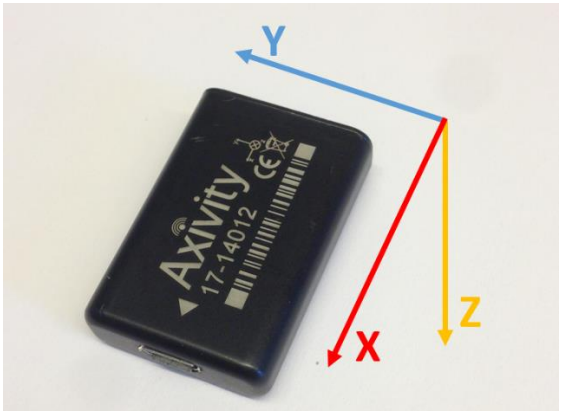


Figure 1. Orientation of the axis of the Axivity AX3 activity monitor.

Protocol

Anthropometric measurements of the participant were taken first. The participants were barefoot and wore shorts. They were then introduced to the equipment to familiarize with it. This included seeing and holding the Metamax mask. Comfortable walking shoes, preferably training shoes were put on before continuing with monitor placement. The monitor was not placed directly on the skin, but on a 5 x 5 cm piece of Fixomull. The side of the monitor with writing was always placed facing the skin with the USB output pointing down. One monitor was placed on L3 on the spinal column and one on the thighs midline, in the middle of the anterior superior iliac spine and the proximal part of patella (Figure 2). The monitor were placed on the least affected leg on the children with CP and the right leg on the TD children. The last monitor was placed on the inside of the measuring wheel. A piece medical tape was put over all the monitors to make sure they did not fall off during testing.

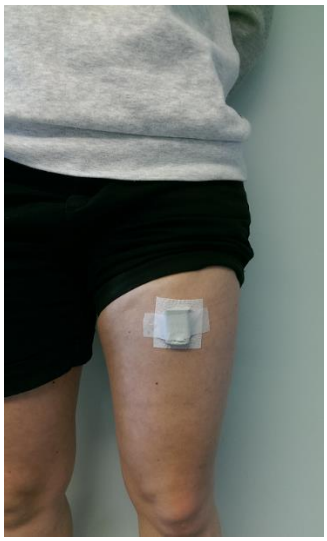
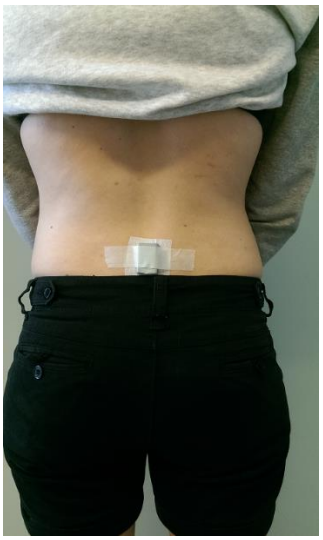
A  B 

Figure 2. Placement of the Axivity AX3 monitor on mid-thigh (A) and L3 on lower back (B).

The chest strap to the heart rate monitor was then attached. Correct size of the Metamax mask was found and attached over the nose and mouth of the participant. To ensure that no air leaked trough the sides of the mask, a hand was held in front of the opening. The participant was asked to draw their breath as hard as they could, and the mask would press in against their cheek if it was attached properly. The rest of the Metamax equipment was carried by the participant on their back (Figure 3). The participant was instructed to walk back and forth for five minutes, on a 46-meter long pathway, in a hallway in the basement of the hospital. They were told to walk at *a normal speed, as they usually walked*. It was emphasized that it was important that they did not talk during testing so the measurements would be accurate. To be able to synchronize the monitors, a heal drop was performed before the participant started walking. This was done by standing still for five seconds before going up on toe and dropping hard down with their heel on the floor, followed by a new five-second period standing still. If the child had problems with going up on toe, they held one of the testers hand or the testers flicked on the monitors. On the testers signal, the participant started walking. The heart rate and Metamax measurements were started simultaneously. One tester walked behind the participant with the measuring wheel and another next to them holding the recording equipment. At each end of the pathway, the participant was told to turn around and to continue walking. During testing, the participants were asked if they felt OK and were instructed to show a "thumb up" or a "thumb down" as a response. If they showed a "thumb down" the test would be stopped and the mask immediately taken off. After the test, the heel drop was repeated. The data was downloaded to the MetaSoft (Cortex Biophysik GmbH, Leipzig, Germany), Polar ProTrainer 5 (Polar Electro Oy, Finland) and Omgui software directly after testing.

Figure 3. A participant ready for testing, wearing Metamax equipment.

Data analysis

A graph with VO_2 and RER values from the five-minute test was made in Excel (Microsoft Excel 2013 version). To ensure that a steady state was reached, the last two minutes of the test were identified. The most stable minute within this period was found, and the VO_2 and RER values for this minute averaged. Relative VO_2, oxygen cost (O_2 cost), EE, relative EE and EC was then estimated from the measured values (Equation 1,2,3,4 and 5).[4,9] Weight in kilogram (kg) was used for the estimations, in addition to walking speed in meters per minute (m/min). Walking speed in meters per second (m/s) and m/min were calculated per pathway length, using the measuring wheel and the monitor placed on it.

Equation 1

$$Relative\ VO_2\ (mL/kg/\text{min}) = \left(\frac{VO_2}{weight}\right) * 1000$$

With VO_2 in L/min

Equation 2

$$O_2\ cost(mL/kg/m) = \frac{Relative\ VO_2}{Walking\ speed}$$

With relative VO_2 in mL/kg/min and walking speed in m/min

Equation 3

$$EE\ (kJ/\text{min}) = \big((4{,}96 * RER) + 16{,}04\big) * relative\ VO_2$$

With relative VO_2 in mL/kg/min

Equation 4

$$Relative\ EE\ (J/\text{kg/min}) = \frac{EE}{weight} * 1000$$

With EE in kJ/min

Equation 5

$$EC\ (J/kg/m) = \frac{Relative\ EE}{Walking\ speed}$$

With relative EE in J/kg/min and walking speed in m/min

Heart rate from the concurrent one-minute period was found and averages using the Polar Trainer 5 software. The accelerometer data was converted in Omgui to a format (.csv file) that could be read in MATLAB (MATLAB R2014a, The MathWorks, Inc., Massachusetts, US) Rest of the data analysis was done using this software. The time of the heal strike before testing was used to identify the starting point of the walking test in the accelerometer data. A time period of six minutes (72 000 samples) after this heal strike was chosen to ensure that the whole five minute period was included. Example of the signal can be seen in Figure 4. The same one minute period as used from the Metamax data was taken out. A ten-second "buffer" was added because of a delay in the Metamax signal compared to the accelerometer signal.

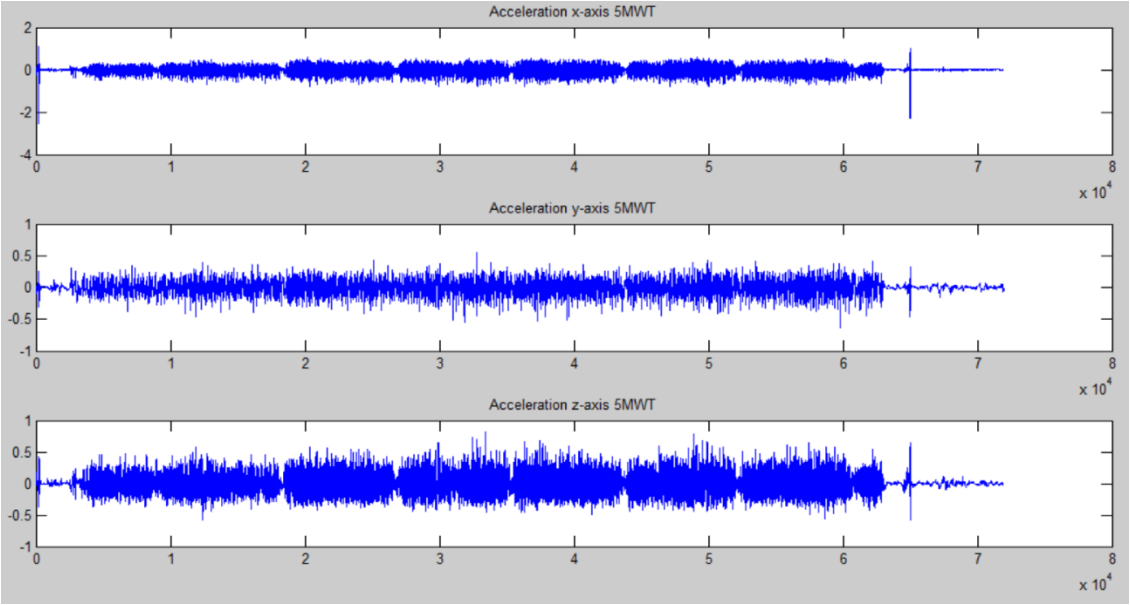


Figure 4. Accelerometer signal from monitor on lower back from the five-minute walking test. The x-axis on the graphs show the number of samples (72 000) and y-axis is sample range in g.

Estimation of energy expenditure

Brandes et al.'s method was followed to estimate the energy expenditure.[26] The raw acceleration signal was filtered using a 4th order recursive butterworth band pass filter (0.1-15Hz) to each axis. Vector magnitude (VM) is used as the input representing the acceleration data in the equations. It gives information about the size of the signal using all three axis (Figure 5). Mean VM for the one-minute period was calculated from the monitor on lower back (Equation 6).

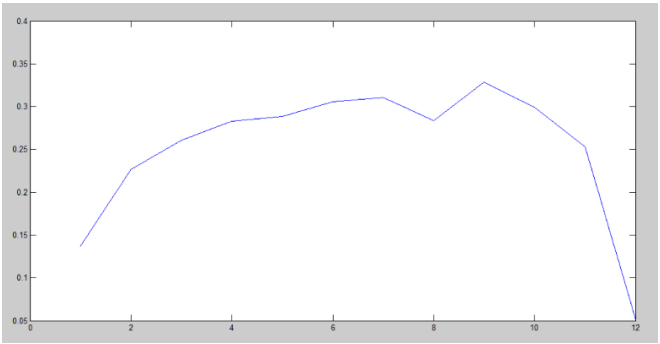


Figure 5. Vector magnitude from monitor placed on lower back during the five-minute walking test. The graphs x-axis show the number of samples and y-axis is sample range in g.

Equation 6

$$Mean\ VM\ (g) = \text{mean}\sqrt{x^2 + y^2 + z^2}$$

Brandes et al. use physical activity related EE as outcome in their equation. This is calculated by subtracting resting EE from total EE. To be able to compare estimated values to indirect calorimetry measurements (total EE), resting EE values were added to the equation. Values measured by Brandes et al. was used, taking the mean of the two age groups 6-11 and 12-17 years (=5.25) and adding it to the equation. Relative resting EE (Equation 4) was calculated using the average weight of the same age groups, and then added to the equation (=107). Weight and VM was then used to estimate EE (Equation 7) and relative EE (Equation 8).

Equation 7

$$EE\ (kJ/min) = \left(-18{,}61 + (0{,}24 * weight) + (53{,}97 * VM)\right) + 5.25$$

Equation 8

$$EE\ relative\ (J/min/kg) = \left(-40{,}19 + (0{,}24 * weight) + (816{,}11 * VM)\right) + 107$$

Estimation of relative VO_2

Using Hildebrand et al.'s method, VM was calculated from the raw acceleration signal from the monitor on lower back.[27] The value of gravity was subtracted from the VM before the negative values were rounded up to zero. (Equation 9).

Equation 9

$$VM\ (g) = (x^2 + y^2 + z^2)^{½} - 1$$

Further reductions in the data was done by calculating the average values per 1-sec epochs. The one-minute period that have been used so far in the analysis was chosen and used to estimate relative VO_2 (Equation 10 and 11).

Equation 10

$$Relative\ VO_2(mL/kg/\text{min}) = 0{,}0498 * (VM * 1000) + 10{,}39$$

Equation 11

$$Relative\ VO_2(mL/kg/\text{min}) = 0{,}0559 * (VM * 1000) + 10{,}03$$

Variation in the acceleration signal

To look at the variation in the signal during the whole test, VM for the five-minute period was calculated using Brandes et al.'s method. Mean, maximum and minimum VM values for the period was then found.

Statistical analysis

All statistical analysis was conducted in IBM SPSS statistics version 22 (SPSS, Inc., Chicago, IL). Normal distribution of the data was examined using Shapiro-Wilk test and visual assessment of histograms and Normal Q-Q plots. Group differences between TD and CP children were tested for all variables with an independent samples t-test. Paired sampled t-test was used to test for differences between indirect calorimetry measured and accelerometer estimated EE. Bland-Altman analysis was used to evaluate the agreement between the two methods. The relationship between the acceleration signal and EE was examined using Spearman correlation. All results are presented in mean ± standard deviation (SD). Significance level was set at $p < 0.05$ for all statistical analysis

RESULTS

From the 22 participants, one TD child was excluded after the data analysis due to suspicion of incorrectly measured VO_2 values. This results in 21 participants. Characteristics of the TD and CP participants can be found in Table 1. Of the six children with CP, two were classified with GMFCS level I, three with level II and one with level III.

Table 1. Participant characteristics for the two groups, with CI and p-value of group differences.

	TD	**CP**	**Group difference**
N (girls/boys)	15 (8/7)	6 (2/4)	
Age (years)	10.0 ± 1.7	12.4 ± 3.9	p = 0.067 CI -4.910 - 0.186
Height (cm)	141.7 ± 12.1	145.3 ±13.8	p = 0.559 CI -16.301 - 0.988
Weight (kg)	35.9 ± 9.6	44.1 ± 21.6	p = 0.236 CI -22.107 - 5.800

During the five-minute walking test, the participants had a walking speed of about 1 m/s, where the TD children walked significantly faster than the children with CP (Table 2). Mean HR, VO_2, EE and VM values were slightly higher for the children with CP, but the difference was not significantly different from the TD children. There was a significant difference between the groups in RER, O_2 cost and EC, with higher mean values measured for the participants with CP.

Table 2. Measured test values from the five minute walking test for the two groups with CI and p-value of group differences.

	TD	CP	Group difference
Walking speed (m/s)	1.1 ± 0.1	0.9 ± 0.3	p = 0.032* CI 0.019 – 0.390
HR (bpm)	105.2 ± 10.8	119.8 ± 31.5	p = 0.120 CI -33.48 – 4.21
VO_2 (L/min)	0.52 ± 0.12	0.73 ± 0.40	p = 0.080 CI -0.44 – 0.03
VO_2 (mL/kg/min)	14.6 ± 2.1	16.6 ± 3.3	p = 0.123 CI -4.50 – 0.58
O_2 cost (mL/kg/m)	0.22 ± 0.04	0.34 ± 0.13	p = 0.002* CI -0.20 – -0,05
RER	0.83 ± 0.06	0.92 ± 0.11	p = 0.040* CI -0.16 – -0.004
EE (kJ/min)	10.4 ± 2.3	14.9 ± 8.7	p = 0.071 CI -9.46 – 0.43
EE (J/kg/min)	295.4 ± 41.7	341.2 ± 67.2	p = 0.071 CI -95.98 – 4.40
EC (J/kg/m)	4.35 ± 0.75	7.06 ± 2.72	p = 0.002* CI -4.27 – -1.16
VM back[1] (g)	0.29 ± 0.05	0.34 ± 0.19	p = 0.240 CI -0.17 – 0.04
VM thigh[1] (g)	0.70 ± 0.13	0.63 ± 0.22	p = 0.354 CI -0.09 – 0.23

HR=heart rate; RER=respiratory exchange ratio; EE=energy expenditure; EC=energy cost; VM=mean vector magnitude
*Significant differences at $p < 0.05$
[1] Estimated using Brandes et al.'s method

Figure 6 presents the results of measured EE and the EE estimations from the acceleration signal, using data from the monitor placed on lower back. EE estimated from the equation developed by Brandes et al. are in general close to the values obtained from indirect calorimetry (Figure 1A). For the TD children the EE is on average underestimated with 0.1% ± 25.9 SD and overestimated with 4.8% ± 46.3 SD for the children with CP. The relative EE values are overestimated in the two groups (Figure 1B). On average, it overestimates with 4.5% ± 17.4 SD for the TD children and 2.3% ± 40.0 SD for the children with CP. Relative VO_2 estimated using Hildebrand et al's equations also generally overestimate the values for the participants (Figure 1C). The first equation overestimate with 12.0% ± 25.5 SD for the TD children, which is statistically different from the measured value ($p = 0.016$). For the children with CP it overestimates with 1.2% ± 29.1 SD. The second equation on average overestimates with 14.1% ± 16.7 SD and 3.4% ± 32.1 SD for the TD children and children with CP. The difference between the measured and estimated values are significantly different for the TD children ($p = 0.006$).

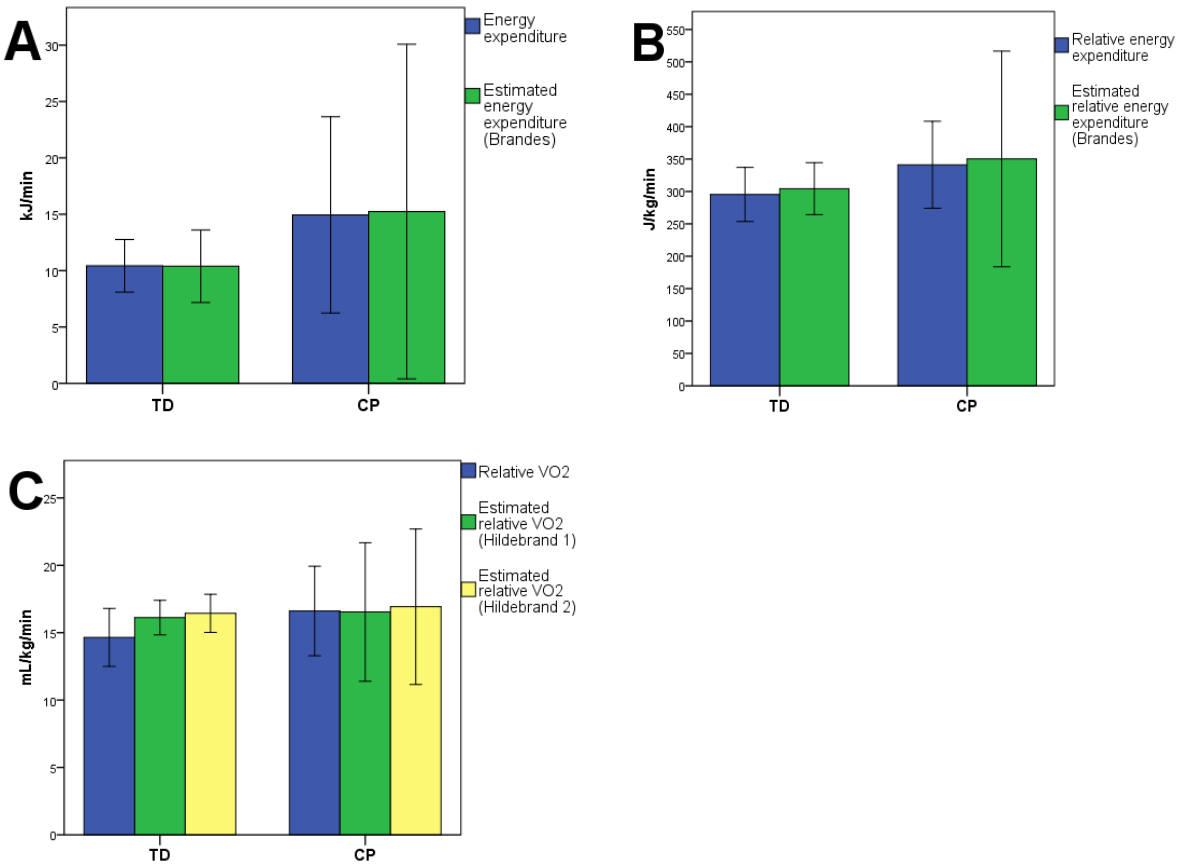


Figure 6 Energy expenditure and relative VO_2 values measured by indirect calorimetry compared to values estimated using Brandes et al (A and B) and Hildebrand et al's (C) equations. Error bars = ± 1 SD.

The accuracy of the estimations on an individual level, and the agreement between indirect calorimetry and the equations used can be seen in Figure 7. The mean differences and limits of agreement in EE is 0.04 kJ/min (-5.1 to 5.2 kJ/min) for TD children and -0.3 kJ/min (-14.9 to 14.3 kJ/min) for the children with CP, -8.9 J/kg/min (-104.4 to 86.7 J/kg/min) in relative EE for TD children and -9.0 J/kg/min (-300.0 to 282.0 J/kg/min) for the children with CP. In EC for TD children it is -0.09 J/kg/m (-1.5 to 1.3 J/kg/m) and 0.4 J/kg/m (-4.8 to 5.5 J/kg/m) for the children with CP. Relative VO_2 for TD children are not included as the two methods gave significantly different values. For the children with CP, mean difference and limit of agreement is 0.06 mL/kg/min (-4.8 to 5.5 mL/kg/min) for relative VO_2.

A lack of agreement between the methods exist if the measurement is outside of the 95% CI. This can be seen in EE (Figure 7A), and EC (Figure 7E) for the TD children. A linear regression analysis found proportional bias among the TD children in EC ($p = 0.023$) and the children with CP in EE ($p = 0.037$) (data not shown).

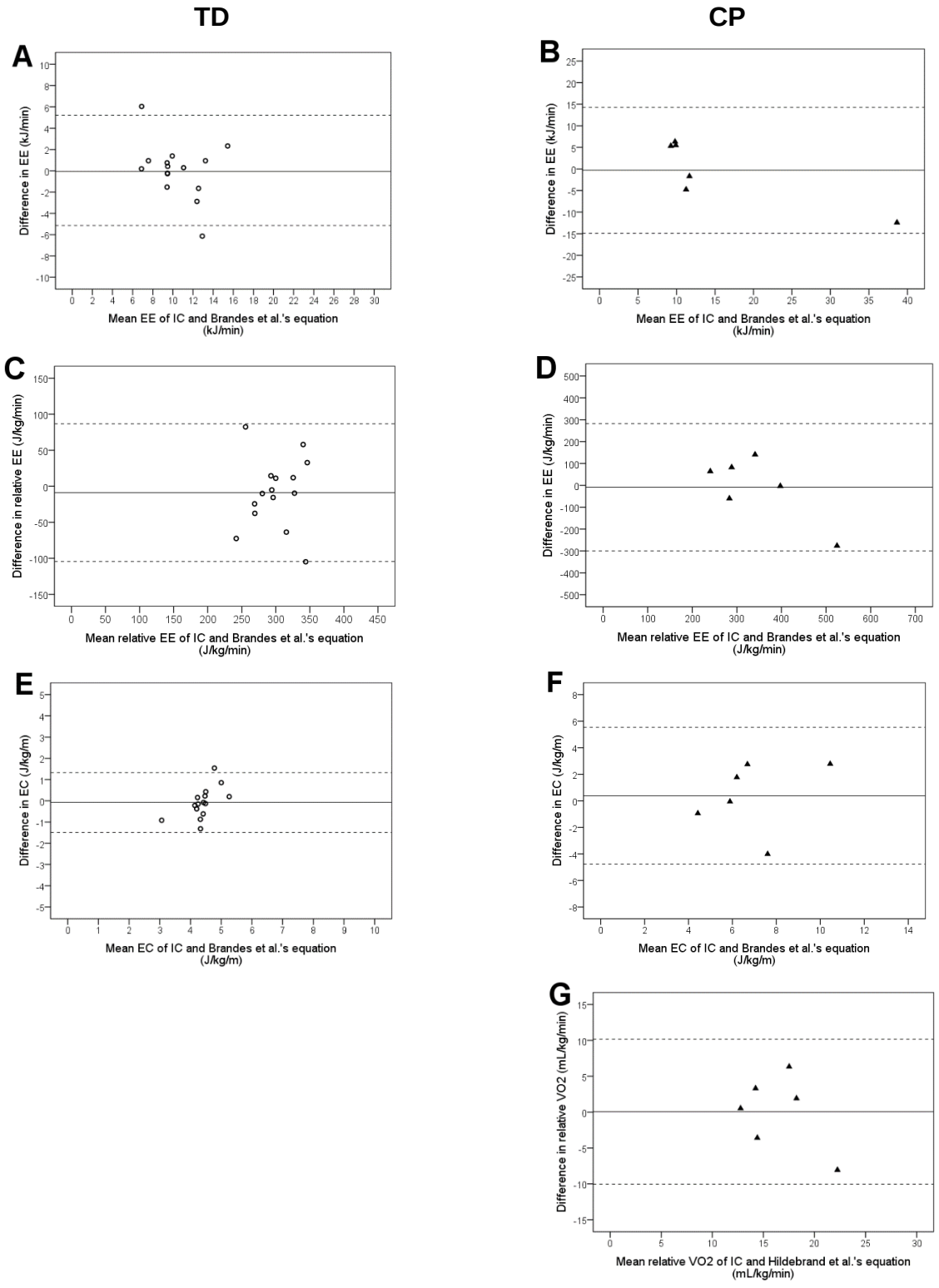


Figure 7 Bland-Altman plots for EE and VO_2 estimations using Brandes et al.'s (A-F) and Hildebrand et al.'s equations (G). Figure G represent both equations from Hildebrand et al. The solid line represent the mean difference between the methods. Broken lines represent 95% limits of agreement (±1.96 SD).
IC=indirect calorimetry

Looking at the relationship between EE values and the acceleration signal, measured EE is not found to correlate with the VM ($r = -0.171$, $p = 0.457$). The use of Brandes et al's equation on the acceleration signal does not improve the relationship to the measured EE ($r = 0.269$, $p = 0.239$). This is also the case for the rest of the measured values. There is not found to be a significant correlation between measured and estimated relative EE ($r = 0.335$, $p = 0.138$) or between the measured relative EE and VM ($r = 0.356$, $p = 0.113$). EC does not correlate with VM ($r = -0.217$, $p = 0.345$) but has a moderate correlation with the estimated EC ($r = 0.492$, $p = 0.023$). The measured relative VO_2 does not correlate wither either of the relative VO_2 estimations or the VM from Hildebrand et al. ($r = 0.356$, $p = 0.113$ for all). Although not statistically significant, the spearman correlation coefficient is higher between measured relative VO_2 and VM calculated using Brandes et al's method ($r= 0.413$, $p = 0.063$).

To examine if the VM (estimated using Brandes et al.'s method) is stable during the whole test period, and if the value from the one minute is representative, the VM from the five minutes was viewed (Figure 8). A mean value of 0.28 g ± 0.376 SD is found for the TD children. They have a mean range of 0.064 g ± 0.036 SD which show little variation during the test period for most of the cases. The children with CP have a mean VM of 0.33 g ± 0.192 for the whole test, with a mean range of 0.082 g ± 0.038 SD. These VM are close to identical to the mean values from the one-minute period represented in Table 1.

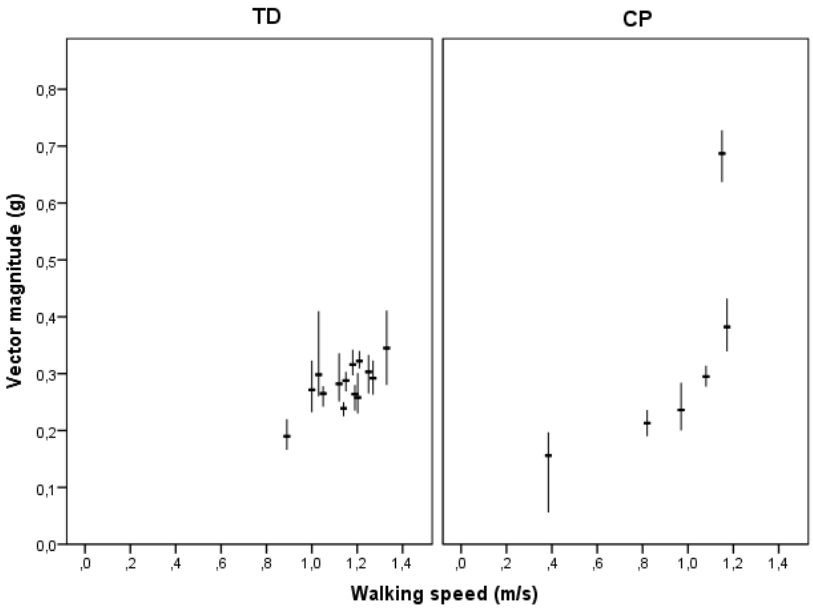


Figure 8 Mean VM (horizontal line) for the acceleration signal (g) with a range of maximum and minimum values. The value represents the whole five minute walking test with TD children presented to the left and children with CP to the right. VM estimated using Brandes et al.'s equation from monitor on lower back.

DISCUSSION

The aim of this study was to use the Axivity AX3 activity monitor to investigate EE in children with CP and TD children during walking, and see if raw acceleration data could be used to estimate EE. The main findings show that by using existing equations[26,27], it is possible to make accurate estimations of EE for the two groups. Relative VO_2 was accurately estimated for the children with CP, but the estimations did not seem to be equivalent to indirect calorimetry for the TD children. The equations does not seem to be suitable for individual estimations, as there is a large variation in the accuracy of the estimations for the participants.

The children with CP were slightly older, higher and heavier than the TD children, but the difference between the groups in these variables were not statistically significant. They also had higher HR, VO_2, EE and VM values from the walking test. Although not statistical different, this difference might be of physiological and clinical importance. According to existing knowledge about children with CP, it was expected to find a significant difference between the groups in EE, with higher values for the children with CP. A possible reason for why this was not found, can be that the children walked at preferred walking speed, which was significantly lower among the children with CP. If they had held the same speed as the TD children, this most likely would have increased their VO_2, and thereby the EE. This is supported by the statistical difference between the groups in EC and O_2 cost, with higher measured values for the children with CP. This indicates that walking speed has an effect on EE.

EE and relative VO_2 estimated by indirect calorimetry measurements (equation 1-5 in methods), will be referred to as measurements to avoid confusion with the EE and VO_2 estimated from the equations by Brandes et al. and Hildebrand et al.

The equations developed by Brandes et al. gave accurate estimations of EE for both groups compared to measurements using indirect calorimetry (underestimation 0.1% for TD and overestimating 4.8% for children with CP). Estimations of relative EE were also relatively accurate (4.5% overestimation for TD and 2.3% for children with CP). A contributing factor for this accuracy is that similar monitor placement on lower back was used by Brandes et al. and in this study. This ensures that the acceleration signal is close in size and shape to the signal used to developed the equation. This should have a positive effect on the accuracy of

the estimations, assuming that the monitor is correctly placed. In their study, Brandes et al. found that the acceleration signal and weight explained 95% of the variation in EE. Those were the only variables used for individual input in the equations.[26] Weight affects the acceleration signal, as larger weight creates a larger acceleration signal. Especially when estimating relative EE, using weight as input is important, since EE is normalized to it. If the participants weight is not used, then this will in most cases decrease the accuracy of the estimation. It is unlikely that the coefficients accounting for weight are a better variable than the actual weight.

Hildebrand et al.' developed equations specific for children, in contrast to Brandes et al. who used data from participants at all ages (8-81). The children with CP and the TD children have similar VO_2, age, height and weight as the children the equation is based on, which should make them suitable. The estimations for the children with CP were on average accurate (1.2% and 3.4% overestimation), but the estimations on TD children were significantly different from the measured values (12.0% and 14.1% overestimation). Although estimating relative VO_2, the equations does not use information about the participants weight. As mentioned above, this can decrease the accuracy of the estimations. Another important point is that the placement of the monitor is different between the testing in this study (lower back) and in Hildebrand et al.'s (hip). Accurately estimations can therefore not be expected. There is more movement in the hip than lower back when walking, which cause a larger VM. This can contribute to explain why the estimations are more accurate for the children with CP. Although not statistically significant, the group have a slightly higher mean VM than TD children (0.34 g vs 0.29 g). Being the only input in the equations (equation 10 and 11), the difference in VM is what causes the difference in relative VO_2.

Bland-Altman plots were used to evaluate the agreement between indirect calorimetry and the use of acceleration data as methods to measure EE and relative VO_2. For the methods to have a high agreement, the data points should lie between the 95% limits of agreement.[30] For the TD children the points are outside of this limit for EE and EC, and for relative EE the points appear to be on the line. All the points meet the requirement of being between the limits of agreement for the children with CP. However, it is important to note that the size of the groups affect the 95% limit. Both the groups are small, but the group of children with CP is especially small, causing the limits to be extremely wide. Outliers in the data are visible, also contributing to the wide range. Being inside the limit of agreement does not mean the

agreement is high enough so that acceleration data can be used to accurately estimate EE, EC and VO_2. For this, limits based on physiological and clinical relevance should be set in advance.[31] With this not being done, a final conclusion cannot be drawn. What can be said, is that the range is too wide to give accurate estimations on an individual level. The closer the points are to 0, the more accurate the estimation is, as the 0 value on the y-axis represent complete agreement between the two measurements. Viewing the plots, it is apparent that the points seem to either over- or underestimate a great deal for most of the participants. Proportional bias was found for TD children in EC and the children with CP in EE, which indicate that the two methods do not agree equally through the range of measures.

A possible reason for the varying accuracy of the estimations on an individual level, is that variables not taken into account in the equations affect the signal. If these were found and implemented, or used to make new models, it could improve the quality of the estimations. Due to little variation in the data in this study, it was not possible to run regression analysis to investigate this further. In addition to finding new variables, the existing correlation coefficients found and used by Brandes et al. and Hildebrand et al. in their equations might need to be adjusted. Brandes et al. estimated physical activity related EE from their equation and not total EE as measured by indirect calorimetry. Resting EE from their study was used to estimate total EE. Even though the groups were similar (weight and height), they were not identical, so it is likely that it affected the estimations. The value added was identical for all, so the distribution of the points relative to each other would remain the same.

EE is activity specific, and Crouter et al. stated that no single regression equation works well across a wide range of activities for the prediction of EE.[32] The equations by Brandes et al. and Hildebrand et al. are not specifically developed just for walking, but the majority of the activities in their protocol were walking at different speeds. This should make the equations more suitable to estimate EE during walking than other activities. However, since other activities also are included, such as cycling, that could decrease the accuracy for walking. Both Brandes et al. and Hildebrand et al. mentioned that the sample the equations are developed from only consisted of healthy participants, and might not be generalizable to those who are obese or certain patient groups. Although not directly mentioned, this could include the children with CP and affect the accuracy of the estimations in that group.

How the information from the accelerometer is processed affects the outcome of the estimations. In this study, VM is used so the methods by Brandes et al. and Hildebrand et al. can be accurately repeated. Little and no correlation was found between VM and the measured and estimated EE, EC and VO_2 values. It is possible that other types of information about the acceleration signal might fit better for EE estimations, such as mean amplitude deviation, root mean square, standard error, peak acceleration or total power. ot In this study, acceleration data from all three axis are used. Some studies claim that it does not give more information than omnidirectional accelerometers that mostly measure in the vertical direction.[17] Others mean that it is the analytic approach that is not good enough yet, but that more comprehensive assessment of body movement can be provided using three axis.[15,33] Since children with CP experience difficulties when walking, using a triaxial accelerometer might be more suitable as it has the possibility to detect movement in different planes. Large movements in other directions than the vertical when walking could indicate the use of more energy. This should therefore be taken into consideration when deciding on what method to use, particularly if participants with CP are included. Another factor that affect the signal is the placement of the accelerometer. Body segments move in different ways when walking and placement should be carefully though trough. In this study one monitor was placed on mid-thigh and one on lower back. As mentioned, result from the latter has been presented. Using the mid-thigh placement might give better individual estimations as there is more variation in this signal. To examine this, the equations need to be modified, as the VM is almost twice the size as the VM from the monitor on lower back. This results in a large overestimation of the EE which is inapplicable to comparison. That two different processing methods were used in thus study highlight the point that by using raw signal you can replicate and compare studies. However, more should be known about what the best processing method is.

For the children with CP, it appears that the VM increase as they walk faster. This is not visible for the TD children, as they are more clustered together. This is not surprising as they all walk on preferred speed, and there is not much difference between the gait in TD children. The trend seen among the children with CP is most likely due the small size, but we also know that there is more variation in that group in gait. VM proved to be relatively stable during the whole test period, as it had a small range for most of the participants. The VM from the one minute period seem to be representative for the whole test period, as the mean values are close. This indicates that it does not matter which period of the test is used, the estimations will results in similar values. This emphasize the main advantage with the use of

accelerometer over VO_2 measurements, that it is no need to consider physiological factors such as reaching steady state. The duration of the test is no longer as important and can be reduced. For children with CP that go through lot of testing, this is important as it can reduce the burden. It also makes it possible to include more tests, for example at more walking speeds, before the child is tired.

Strengths and limitations

Indirect calorimetry is considered as the gold standard for measuring VO_2 and the comparison of the estimated values to this give precise information about their accuracy. Calibration of the equipment and instructions were given by the same person every time, to ensure that it took place the same way. Testing two groups that are known to be different from each other can be a strength if the methods are good enough to detect these differences. However, only six children with CP were tested, which makes it a small group. The variation that exist among the individuals in this population is most likely not represented. This must be taken into consideration when interpreting the results. The statistical strength is not as high and the findings not as generalizable for children with CP. The protocol only consisted of one walking speed which gave low variation in the data. For this reason it was not possible to test if other variables affected the acceleration signal.

Relevance of findings

The relatively accurate estimations on group level makes it possible to use raw acceleration data to estimate EE in larger group studies or on populations similar to the one tested here.

Further research

The focus of future studies should be to improve the individual estimations. To further investigate the effect walking speed has on EE, different walking speeds should be included. This will also cause more variation in the data, which is required for using regression analysis to examine if other variables should be included in the equations. EE is activity specific and there is a need to look at other activities as well if we want to say something about the EE used there. Larger groups should be investigated, especially for children with CP, so that the agreement between indirect calorimetry and the use of acceleration data to estimate EE can be found.

Conclusion

The use of raw acceleration data seem to be equivalent to indirect calorimetry when estimating EE on a group level, if appropriate equations are used. Accurate estimations of EE and relative EE can be made for TD children and children with CP during walking. Relative VO_2 can also be accurately estimated for children with CP, but it does not seem to be appropriate for TD children as it overestimates. On an individual level, there is large variation in the accuracy of estimated EE, and the equations used do not appear to be suitable. This needs to be addressed in future studies, in addition to testing a larger sample of children with CP.

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